METHOD FOR REDUCTION OF CELL VIABILITY BY COLD PLASMA TREATMENT ON BREAST CANCERS BASED ON MOLECULAR PROFILING

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims the benefit of the filing date of U.S. Provisional Patent Application Ser. No. 62/953,767 filed by the present inventors on Dec. 26, 2019.

[0002] The aforementioned provisional patent application is hereby incorporated by reference in its entirety.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0003] None.

BACKGROUND OF THE INVENTION

Field of the Invention

[0004] The present invention relates to systems and methods for treating cancer with cold atmospheric plasma.

Brief Description of the Related Art

[0005] Among women worldwide, breast cancer is the most frequently diagnosed cancer and the most common cause of cancer death. Bray, F., et al., *Global cancer statistics* 2018*: GLOBOCAN estimates of incidence and mortality worldwide for* 36 *cancers in* 185 *countries*. CA Cancer J Clin, 2018. 68(6): p. 394-424. The major breast cancer molecular subtypes are based on estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) expression. Howlader, N., et al., *Differences in Breast Cancer Survival by Molecular Subtypes in the United States*. Cancer Epidemiology, Biomarkers & Prevention, 2018. 27(6): p. 619-626. With a total of eight combinations of ER, PR and HER2 expression (see Bauer, K., C. Parise, and V. Caggiano, *Use of ER/PR/HER2 subtypes in conjunction with the* 2007 *St Gallen Consensus Statement for early breast cancer*. BMC Cancer, 2010. 10), breast cancer is acknowledged as a highly complex disease. Molecular profiling, however, can provide information on disease prognosis and therapeutic approach. Kittaneh, M., A. J. Montero, and S. Gluck, *Molecular profiling for breast cancer: a comprehensive review*. Biomark Cancer, 2013. 5: p. 61-70; Duffy, M. J., et al., *Clinical use of biomarkers in breast cancer: Updated guidelines from the European Group on Tumor Markers (EGTM)*. Eur J Cancer, 2017. 75: p. 284-298 N Approximately 75% of breast cancers are ER-positive (ER+) while 55-65% are PR-positive (PR+). See Anderson, W. F., et al., *Estrogen receptor breast cancer phenotypes in the Surveillance, Epidemiology, and End Results database*. Breast Cancer Research and Treatment, 2002. 76(1): p. 27-36; Colditz, G. A., et al., *Risk factors for breast cancer according to estrogen and progesterone receptor status*. J Natl Cancer Inst, 2004. 96(3): p. 218-28; and Nadji, M., et al., *Immunohistochemistry of estrogen and progesterone receptors reconsidered: experience with* 5,993 *breast cancers*. Am J Clin Pathol, 2005. 123(1): p. 21-7.

[0006] Survival rates of patients are highest with ER+/PR+ tumors, intermediate with either ER+/PR− or ER−/PR+ tumors, and lowest with ER−/PR− tumors. Alanko, A., et al., *Significance of Estrogen and Progesterone Receptors, Disease-Free Interval, and Site of First Metastasis on Survival of Breast Cancer Patients*. Cancer, 1985. 56(7): p. 1696-700

[0007] Several studies have reported changes in hormone receptor status between primary and metastatic breast cancer with discordance rates estimated to be 20% for ER and 40% for PR (both of which are higher than HER2 discordance rate). See, Curtit, E., et al., *Discordances in estrogen receptor status, progesterone receptor status, and HER2 status between primary breast cancer and metastasis*. Oncologist, 2013. 18(6): p. 667-74; RJ, B., et al., *Changes in Estrogen Receptor, Progesterone Receptor and Her-2/neu Status with Time: Discordance Rates Between Primary and Metastatic Breast Cancer*. Anticancer Research, 2009. 29(5): p. 1557-62; Sighoko, D., et al., *Discordance in hormone receptor status among primary, metastatic, and second primary breast cancers: biological difference or misclassification*? Oncologist, 2014. 19(6): p. 592-601; and Liedtke, C., et al., *Prognostic impact of discordance between triple-receptor measurements in primary and recurrent breast cancer*. Ann Oncol, 2009. 20(12): p. 1953-8. Patients with discordant receptor status have lower rates of survival than patients with consistent receptor status possibly due ineffective therapeutic interventions compared to patients with consistent receptor status. Tamoxifen, a selective estrogen-receptor modulator, reduces risk of disease recurrence by 47% after 5 years and mortality by 26% after 10 years in ER+ patients (Riggs, B. L. and L. C. Hartmann, *Selective estrogen-receptor modulators*—mechanisms of action and application to clinical practice. N Engl J Med, 2003. 348(7): p. 618-29) but increases the risk for thromboembolic events significantly (Pritchard, K. I., et al., *Increased Thromboembolic Complications with Concurrent Tamoxifen and Chemotherapy in a Randomized Trial of Adjuvant Therapy for Women with Breast Cancer*. Journal of Clinical Oncology, 1996. 14(10): p. 2731-7) and absence of ER expression is associated with de novo resistance to tamoxifen (Johnston, S. R. D., et al., *Changes in Estrogen Receptor, Progesterone Receptor, and pS2 Expression in Tamoxifen-resistant Human Breast Cancer*. Cancer Research, 1995. 55(15): p. 3331-8). In comparison, patients treated with letrozole, an aromatase inhibitor, had a lower chance of relapse over a 5-year period but reported increased incidences of adverse events. Coates, A. S., et al., *Five years of letrozole compared with tamoxifen as initial adjuvant therapy for postmenopausal women with endocrine-responsive early breast cancer: update of study BIG* 1-98. J Clin Oncol, 2007. 25(5): p. 486-92.

[0008] HER2 amplification (HER2+) occurs in approximately 25-30% of primary human breast cancers and is the most significant prognostic factor compared to other factors such as ER, PR, tumor size, and age. See, Slamon, D. J., et al., *Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene*. Science, 1987. 235(4785): p. 177-82; and Slamon, D. J., et al., *Studies of the HER-2/neu proto-oncogene in human breast and ovarian cancer*. Science, 1989. 244(4905): p. 707-12. HER2, in addition to other human epidermal growth factor (hEGF) receptors, is involved in a complex network of pathways that are responsible for signaling normal cellular processes such as cell growth, migration, differentiation, and death. Yarden, Y. and M. X. Sliwkowski, *Untangling the ErbB signaling network*. Nature Reviews Molecular Cell Biology, 2001. 2(2): p. pages 127-137. An overexpression of HER2, therefore, promotes aggressive tumor behavior which is characterized by significantly decreased rates of